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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,168	02/22/2005	Christopher R. Yonan	06056-0313US1	5885

23973 7590 09/30/2008

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EXAMINER

HANLEY, SUSAN MARIE

ART UNIT	PAPER NUMBER
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1651

MAIL DATE	DELIVERY MODE
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09/30/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/525,168	Applicant(s) YONAN ET AL.	
	Examiner SUSAN HANLEY	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DEAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/30/08 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawal of Rejections

The rejections not explicitly restated below are withdrawn due to Applicant's response in the amendment filed 7/30/08.

Claims 1-17 remain under examination.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention. The independent claims have been amendment to recite the limitation "about 2 ng". This new limitation is held to be NEW MATTER because it contains species (e.g., other amounts of the stained protein) that were never envisaged by the specification as-filed.

The specification discloses that 2 ng of the stained protein are visually observable (p. 7, 18 and 19). The specification does not teach any variation in this number. The newly claimed limitation "about 2 ng" lacks basis in the original disclosure. The use of the word "about" means that there is variation for the amount of protein that is visually observable. Thus, 500 ng of stained protein falls within the claimed range of "about 2 ng". However, the specification does not teach this, or any other, species related to the amount of stained protein that is visually observable.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the claims recite that the formula I encompasses numerous compounds that serve as staining reagents for proteins, wherein about 2 ng of the stained protein is visually observable. However, the specification discloses that only Reactive Brown 10 is described as being capable of the claimed sensitivity. Therefore, neither the specification nor the prior art provide written description for any other

compounds embodied within formula 1 as having the claimed sensitivity. Moreover, the sole example of using Reactive Brown 10 does not provide a representative sample of compounds of formula I having the claimed sensitivity. The specification discloses that the detection limit of Reactive Brown 10 (2 ng) is an unexpected result. However, the claims encompass a multitude of compounds embodied by formula I that are neither contemplated nor disclosed by the as-filed disclosure to possess the disclosed sensitivity. Hence, it is clear that applicant was not in possession of the full scope of the claimed subject matter at the time of filing.

Claim Rejections - 35 USC § 102

Response to Arguments and the Addition of Claims 16 and 17 to the Rejection

Claims 14-17 are under 35 U.S.C. 102(a) as being clearly anticipated by Bayramoglu et al. (July, 2002).

Applicant argues (relating to claims 14 and 15) that the rejection should be withdrawn because Bayramoglu discloses membranes that are conjugated to Procion Brown MX-5BR. Applicant asserts that a dye-conjugated membrane can not be destained since it is covalently attached to the dye.

Applicant's argument is found persuasive for claims 6 and 7 since the composition requires a protein already bound to a protein binding membrane. However, Applicant's assertions are not persuasive regarding claims 14 and 15 because the reference teaches that the membrane and the dye were separate materials that were brought together to make the dye-immobilized membrane (p.2325, left col., 1st

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paragraph). As previously discussed, a kit is a collection of articles. The gathering of these articles, a protein binding membrane and Reactive Brown MX-5BR, by Bayramoglu meets the limitations of a kit.

Regarding claims 16 and 17, Bayramoglu also discloses five standard solutions, each having a known concentration, of lysozyme (Fig. 5). This disclosure fulfills the limitation of claim 16 that recites a set of one or more solutions of a protein standard of known concentrations. As discussed supra, a kit is a collection of articles. The gathering of these articles, a protein binding membrane, Procion Brown MX-5BR and a set of protein standards, as disclosed by Bayramoglu, meets the limitations of a kit according to claim 17.

The claims recite that the protein-binding membrane is capable of being destained. Bayramoglu discloses that the dye-immobilized membrane was prepared by conjugation and then washed (p.2325, left col., 1st paragraph). On page 2328, right col., first paragraph, it is disclosed that the prepared membranes did not exhibit the loss of dye or metal ions from leakage. Bayramoglu concludes that the washing procedure (during membrane preparation) was satisfactory for the removal of *physically absorbed* dye molecules. Hence, non-conjugated dye was removed or destained from the membrane.

The newly added limitations related to the capability of the staining reagent to make about 2 ng of a protein visually observable on the membrane is an inherent result of bringing the membrane-binding protein, protein and dye together.

Response to Arguments

Claim Rejections - 35 USC § 103

Claims 1-17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Alam (US 6,174,729) in view of Hopwood et al. (1973) and Miyagi et al. (1975; abstract only).

Applicant states that a *prima facie* case of obviousness has not been established. This response was argued in Applicant's previous response. Applicant argues that the examiner is discounting the superior results obtained by the claimed composition and methods. Applicant submits that the lack of structural basis among the Procion dyes is discounted and that one of ordinary skill in the art would not expect the structural dissimilarities between the mono-chloro- and di-chloro-compounds to result in different properties. Applicant alleges unexpected results based on the comparison of the sensitivities of the dyes taught by Miyagi and the instantly disclosed dyes and states that Reactive Brown 10 is 10- to 250-fold more sensitive than the comparison dyes. Applicant concludes that neither Alam nor Hopwood discuss the relative sensitivity of Procion dyes and that the increased sensitivity of Reactive Brown 10 relative to Coomassie Blue is unexpected and overcomes the rejection.

Applicant's arguments have been considered but are non-persuasive.

Responding to Applicant's argument that a *prima facie* case was not established in the original rejection and that the structures of Reactive Brown 10 (which is claimed), Coomassie Blue and Procion Blue M-RS used by Miyagi are too dissimilar to suggest a change in the dyes used by Alam to a compound of formula I and that the ordinary

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artisan would not be motivated to make the necessary molecule modifications to achieve the claimed invention, the concept that ties the references together is that Alam teaches that the spotted membrane can be stained with any dye known to bind proteins to produce a visible spot (emphasis added). Alam teaches that Coomassie blue is a typical dye (col. 7, lines 43-57), but not the only dye. Hence, the only requirement to practice the method of Alam is that the dye is known to bind proteins. Therefore, close structural similarity of dyes is not the basis that the ordinary artisan would use to select a dye to practice the method of Alam. The only prerequisite is that the dye is able to bind proteins. Miyagi demonstrates the equivalence of several dyes (including Coomassie Blue (used by Alam) and Procion Blue M-RS for this purpose. Therefore, Miyagi makes a direct comparison between Coomassie Blue and a Procion dye. Hence, the ordinary artisan would have recognized that a comparison between Coomassie Blue and a Procion dye is established by the prior art. Responding to Applicant's argument that the Procion blue M-RS used by Miyagi has little structural resemblance to a compound of formula I, including reactive Brown 10, the name "Procion" is an art recognized term for dyes having monochloro- or dichloro- triazine dyes that are connected to a chromophore (Hopwood, top of page 392). Thus, it is the triazine ring having at least one chlorine atom bound thereto that is common to a compound of formula I, Procion Blue M-RS (taught by Miyagi) and those dyes disclosed by Hopwood on page 392. Fu

Therefore, the ordinary artisan would have known that Procion dyes, including a compound of formula I such as Reactive Brown 10 are known to bind proteins. This is

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the only prerequisite for the method of Alam. The commonality among the Procion dyes is the monochloro- or dichloro- triazine ring and that the ordinary artisan would have recognized from Hopwood that there are a finite number of such dyes that bind proteins, including Reactive Brown 10. Therefore, the ordinary artisan is not required to make molecular adjustments to Coomassie Blue in the method of Alam to arrive at the claimed invention. Rather, the ordinary artisan is only required to select a dye that is known to bind proteins. However, the disclosure by Miyagi clearly makes a connection in the comparison between Coomassie Blue and Procion Blue M-RS. Thus, the ordinary artisan would be motivated to compare other Procion dyes to Coomassie blue. Procion dyes are a class of dyes that bind proteins and Hopwood provides a finite number of Procion dyes, including Reactive Brown 10, from which the ordinary artisan could select to practice the instant invention.

Responding to Applicant's assertion that the sensitivity of Reactive Brown 10 compared to the disclosed dyes is an unexpected result, it is noted that the claims have been amended to read "about 2 ng". In the NEW MATTER rejection, it was noted that this limitation lacks basis in the original disclosure. The use of the word "about" means that there is variation for the amount of protein that is visually observable. Thus, 500 ng of stained protein falls within the claimed range of "about 2 ng". Therefore, the claims are not limited to the embodiment of 2 ng which is alleged to be an unexpected result. The use of the word "about" allows for a very broad range of detection limits and the ordinary artisan would have had a reasonable expectation that the detection limit of

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reactive Brown 10 would be similar to those of Miyagi (100 to 500 ng). These amounts are embodiments that clearly fall within the range of “about 2 ng”.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to [redacted] whose telephone number is (571)272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susan Hanley/
Examiner, Art Unit 1651

/Sandra Saucier/
Primary Examiner, Art Unit 1651